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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WINKLER, ULRIKE	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 06/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/926,799	TAKEDA ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Ocotber 2, 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *5 and 7-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the petition filed by Applicants on October 2, 2003. The petition was granted on January 6, 2003, vacating the prior office action. The Restriction requirement among Groups I-XI is withdrawn and the groups are rejoined.

Sequence listing

Applicant's CRF and paper sequence listing have been entered.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, Paper No. 3 and 6, was sent in the action of July 2, 2003, Paper No. 13.

Drawings

The drawings are have been approved by the Draftsperson.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims make reference to "partial peptides thereof", it is not clear from the claim construction which partial peptides are intended. Does "partial peptides thereof" encompass the common structural elements with other viruses or does it encompass those

sequences that do not share common structure with other viruses. Also, do the "partial peptides" only have to have 80% sequence similarity? In order to distinguish the instant antibodies from those antibodies disclosed in the prior art the "partial peptides thereof" must be more clearly defined. The smallest peptide that can consistently elicit antibodies that recognize the original protein is a peptide that is 6 amino acids in length. Therefore, any polyclonal antibody that is directed at a protein that has minimally 6 amino acids in common with SEQ ID NO:1-11 would fall within the scope of the claim.

Claims 1-4 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear what components are part of the kit, are the antibodies the components of the kit "antibodies against SRSV related virus" or are the peptides listed in the claims part of the kit. Clarification of what is in the kit is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed

invention. The claims are drawn to an antibody against SSRV-related virus, the virus contains polypeptides having at least 80% sequence identity to the polypeptide encoding SEQ ID NO: 1-11 and "partial peptides thereof". The claims do not require that the protein possesses any particular distinguishing feature, biologic activity, or conserved structure. Therefore, the claims are drawn to a genus of polypeptides that are defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is no identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method

of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, the instant invention meets the written description requirement only for those isolated polypeptides comprising the full length amino acid sequence set forth in SEQ ID NO: 1-11. The instant invention does not meet requirement of the written description provision of 35 U.S.C. §112, first paragraph for the full breadth of the claims. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-4 and rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polyclonal antibodies that were produced by injecting a rabbit with a mixture of SRSV virus like particles (see specification page 29, lines15-25; example 5) , does not reasonably provide enablement for monoclonal antibodies or antibodies obtained using partial peptides of the sequences set out in SEQ ID NO 1-11 or sequences or partial peptides that are 80% homology to SEQ ID NO: 1-11. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims are interpreted to be a composition comprising antibodies wherein the antibodies of the kit recognize the peptides of SEQ ID NO: 1 –11.

The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Antibodies recognize epitopes, in this instance it is not clear what specific epitopes the antibodies of the instant claims are to recognize.

Paul (Fundamental Immunology, Raven Press, New York, NY; 1993, 3rd Edition, pg. 251, column 1, lines 11-12) states that immunogenicity is limited by self-tolerance, and that the repertoire of potential antigenic sites in a given polypeptide is a specific for the host organism. Paul also teaches (supra, pg. 249, column 2, lines 10-13) that to determine the immunogenicity of certain regions of a protein, knowledge of the three dimensional structure of the protein is required to determine which polypeptides in a given protein would be accessible on the surface of the protein in order for the putative antigenic determinant to be bound by the antibody. In addition, Paul states that mobility of the putative antigenic determinant within the native protein structure is also a determining factor for the binding of the antigenic determinant to an antibody.

Paul points out (supra, pg. 250, lines 4-8) that "Measurement of the mobility in the native protein is largely dependent on the availability of a high resolution crystal structure, so its applicability is limited to only a small subset of proteins." The determination of an "epitope" is clearly a non-trivial enterprise, coupled with the lack of working examples in the specification, it would require undue experimentation for one of skill in the art to make and use the invention as claimed.

Changes in the amino acid sequence of an antigen can have a direct effect on the ability of the antibody to bind the protein, furthermore, the changes that effect the antibody binding do not have to occur within the epitope binding region (Abaza et al. Journal of Protein Chemistry, 1992, and Nuss et al. Journal of Molecular medicines, 1994)

The smallest synthetic peptide that will consistently produce elicit antibodies are 6 residues in length, smaller peptides may produce weak antibodies (see Harlow D.L. Antibodies: A laboratory manual. Cold Spring Harbor Laboratories Publications, Cold Spring Harbor, NY ed. Harlow et al., page 76). It is also important to consider if the antibody needs to recognize native protein, larger peptides, may be necessary and this has to do with the three dimensional presentation requirements.

The level of one of ordinary skill, although it is well within the skill of those in the art to create a recombinant mutations in a protein sequence and to determine a sequence that may have 80% homology within the sequences set out in SEQ ID NO: 1-11 what is not within the knowledge of the ordinary artisan is to predict what changes in a sequence are permissible and allow the antibody to still bind to the protein. This would require undue experimentation for the

ordinary artisan to determine which mutation would be permissible for the antibody to continue to bind the protein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Matson et al. (WO 94/05700).

The instant invention is drawn to a detection kit comprising antibodies. Specifically an antibody that recognizes the peptides of SEQ ID NO:1-11. The antibody recognizes sequences having 80% homology with SEQ ID NO:1-11 and "partial peptides thereof". The antibodies have been prepared by immunizing with virus-like particles, the detection kit can distinguish different serotypes and genotypes. Note for antibodies to recognize a particular sequence requires that a few epitopes be in common, the claims are directed to antibodies that recognize the "partial peptide thereof". Furthermore, it is not clear whether the "partial peptide thereof" needs to have the exact sequence in common with SEQ ID NO 1-11 or if the "partial peptides" may be as low as 80% sequence similarity.

Matson et al. discloses that individual proteins, particles or proteins aggregates formed from expression of one or more Norwalk virus genes in any prokaryote or eucaryotic expression system are used as an immunogen or inoculate animal to produce polyclonal and monoclonal antibodies for diagnostic assays to detect viral antigens (see pages 34-35, example 9). The comparison of capsid sequences of Norwalk virus and Norwalk-related virus permits the identification of conserved regions of the capsid protein and use of the fragments of such sequences to immunize animals which can result in the production of antisera with more broad reactivity to Norwalk related virus (page 35, lines 10-15). Because of sequence conservation the antibodies may detect many other Norwalk related virus. (page 35, lines 27-29). The antibody can be used in ELISA assay to detect viral antigens (page 35, lines 20-23). The reference discloses the use of kits to detect immune response to Norwalk virus (see page 38, example 13; table 4 and claims 103-106). The term "fragment" is used to define any portion of the protein that can produce an immune response (polyclonal or monoclonal). It is possible that peptides of only 5 amino acids are enough to be immunogenic (see page 11, lines 10-19). The reference indirectly discloses that the choice of sequences that are unique to a particular sequence will result in antibodies that are specific to the individual virus (see page 35, lines 10-19). The reference discloses SEQ ID NO 3 which has sufficient similarity at the level of the "partial peptid"e sequence to read on the instantly claimed invention.

Therefore, the instant invention is anticipated by Matson et al.

Claims 1-4 and 6 rejected under 35 U.S.C. 102(e) as being anticipated by Estes et al. (U.S. Pat. No. 6,572,862 B1).

The instant invention is drawn to a detection kit comprising antibodies. Specifically an antibody that recognizes the peptides of SEQ ID NO:1-11. The antibody recognizes sequences having 80% homology with SEQ ID NO:1-11 and "partial peptides thereof". The antibodies have been prepared by immunizing with virus-like particles, the detection kit can distinguish different serotypes and genotypes. Note for antibodies to recognize a particular sequence requires that a few epitopes be in common, the claims are directed to antibodies that recognize the "partial peptide thereof". Furthermore, it is not clear whether the "partial peptide thereof" needs to have the exact sequence in common with SEQ ID NO 1-11 or if the "partial peptides" may be as low as 80% sequence similarity.

Estes et al. discloses the production of antibodies (see example 6, columns 12-13 and example 9 and table 3) from protein(s) encoded in the cDNA fragments or derivatives thereof, is produced in a prokaryotic or eukaryotic expression system and used to immunize animals to produce polyclonal antibodies for diagnostic assay. Alternatively, synthetic peptides of greater than 15 amino acids made to match the amino acid sequence deduced from the partial cDNA sequence (or from other sequences determined by sequencing additional cDNAs detected with the original or other clones) are used to immunize animals to produce polyclonal antibodies for diagnostic tests. Reactivities with the expressed protein or synthetic peptides show specificity of the polyclonal sera. Reactivities with other viruses in the Norwalk group (Snow Mountain Agent, Hawaii Agent, Taunton Agent, etc.) indicate production of a reagent that recognizes cross-reacting epitopes. Analysis of the deduced amino acid sequence of the Norwalk virus genome has shown that the Norwalk virus has the genetic organization shown in FIG. 10. Based on this information, one can express the complete genome or subgenomic regions of the genome to

produce diagnostic assays to detect viral antigens or immune responses to specific regions of the genome. This information can be used to detect the Norwalk virus, antigens or immune responses to Norwalk virus. This information also can be used to detect other similar currently uncharacterized viruses that cause gastroenteritis or possibly other diseases. Some of these viruses will be in the Caliciviridae or in the picorna virus superfamily. All of these viruses will have matching or similar genomic regions in their DNA sequences. The reference discloses SEQ ID NO 3 which has sufficient similarity at the level of the partial peptide sequence to read on the instantly claimed invention.

Therefore, the instant invention is anticipated by Estes et al.

Claims 1-4 and 6 rejected under 35 U.S.C. 102(e) as being anticipated by Estes et al. (U.S. Pat. No. 6,156,833).

The instant invention is drawn to a detection kit comprising antibodies. Specifically an antibody that recognizes the peptides of SEQ ID NO:1-11. The antibody recognizes sequences having 80% homology with SEQ ID NO:1-11 and "partial peptides thereof". The antibodies have been prepared by immunizing with virus-like particles, the detection kit can distinguish different serotypes and genotypes. Note for antibodies to recognize a particular sequence requires that a few epitopes be in common, the claims are directed to antibodies that recognize the "partial peptide thereof". Furthermore, it is not clear whether the "partial peptide thereof" needs to have the exact sequence in common with SEQ ID NO 1-11 or if the "partial peptides" may be as low as 80% sequence similarity.

Estes et al. discloses the production of antibodies (see claims and example 6) from protein(s) encoded in the cDNA fragments or derivatives thereof, is produced in a prokaryotic or eukaryotic expression system and used to immunize animals to produce polyclonal antibodies for diagnostic assay. Alternatively, synthetic peptides of greater than 15 amino acids made to match the amino acid sequence deduced from the partial cDNA sequence (or from other sequences determined by sequencing additional cDNAs detected with the original or other clones) are used to immunize animals to produce polyclonal antibodies for diagnostic tests. The reference indirectly discloses that the choice of sequences that are unique to a particular sequence will result in antibodies that are specific to the individual virus (see page column 24, lines 19-28). The refence discloses SEQ ID NO 3 which has sufficient similarity at the level of the partial peptide sequence to read on the instantly claimed invention.

Therefore, the instant invention is anticipated by Estes et al.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Lew et al. (Virology 1994).

The instant invention is drawn to a detection kit comprising antibodies. Specifically an antibody that recognizes the peptide of SEQ ID NO:1-11. The antibody recognizes sequences having 80% homology with SEQ ID NO:1-11 and "partial peptides thereof". The antibodies have been prepared by immunizing with virus-like particles, the detection kit can distinguish different serotypes and genotypes. Note for antibodies to recognize a particular sequence requires that a few epitopes be in common, the claims are directed to antibodies the recognize the "partial peptide thereof". Furthermore, it is not clear whether the partial peptide thereof need

only to have 80% sequence similarity with the partial peptide. Claim 2 is a product-by process claim for this Office action, the claim was interpreted as "a composition of matter" (which are *products*). Product-by- process claims are not limited to the manipulations of the recited steps, only to the structure implied by the steps. M.P.E.P. Section 2113.

Lew et al. discloses using serum, which is a collection of antibodies, from patients that have been infected with a virus for the formulation of an immunoprecipitation assay to detect virus in a sample (see figure 3). The reference discloses that there are unique sequences between Desert Shield virus and Norwalk virus (see page 324, paragraph 2) allowing for the distinction between the viruses, yet there are many similar sequences that allow t=for the detection of both viruses within the same assay. Therefore, the instant invention is anticipated by Lew et al.

Conclusion

No claims allowed.

Papers related this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989). The Group 1600 Official Fax number is: (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912.

The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.

ULRIKE WINKLER, PHD.
PATENT EXAMINER 6/22/04